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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

BLANCHARD, DAVID J

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 03/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

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Office Action Summary

Application No.

09/230,111

Applicant(s)

SATO ET AL.

Examiner

David J. Blanchard

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 December 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 122-132, 140 and 142-154 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 122-132, 140 and 142-154 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Claims 1-121, 133-139 and 141 have been cancelled.
Claims 122, 125-129, 132 and 140 have been amended.
Claims 142-154 have been added.
2. Claims 122-132, 140 and 142-154 are pending and under examination.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.
4. This Office Action contains New Grounds of Rejections.

Objections/Rejections Withdrawn

5. All previous rejections applied to claims 121 and 141 are withdrawn in view of the cancellation of the claims.
6. The rejection of claims 121-132 and 140-141, part b, under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.
7. The rejection of claims 121-132 and 140-141 under 35 U.S.C 112, first paragraph, new matter, as containing subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention is withdrawn in view of the amendments to the claims.

8. The rejection of claims 140-141 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn in view of applicant's arguments and the amendments to the claims.

Response to Arguments

9. The rejection of claims 122-132, 140 and applied to newly added claims 142-154 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained (item no. 11, part a of the previous Office Action).

The response filed 12/27/2004 has been carefully considered, but is deemed not to be persuasive. The response states that claim 121 has been cancelled and corresponding new claims 142 and 143 clearly point out and state the claimed subject matter, thereby obviating the examiner's rejection. The response also points to pages 24-25 of the specification where a method for screening for candidate compounds is disclosed and at page 27 where compounds such as Ac-SLV and Ac-SLY were successfully used to disrupt the interaction between Fas (i.e., signal-transducing protein) and FAP-1 (i.e., cytoplasmic protein). In response, the specification as pointed to by applicant is clear in that it discloses a method of identifying a compound that inhibits the interaction between Fas and FAP-1, which is a very different method than what is actually claimed. First, the claims recite a method of identifying an agent that

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inhibits the interaction between a signal-transducing protein and a cytoplasmic protein, which is consistent with the specification as pointed to by applicant. However, part (a) of claims 142 and 143 recite a "compound previously shown to be able to displace the signal-transducing protein bound to the cytoplasmic protein...", which is a component that is not in the specification as pointed to by applicant. Again, the claimed method is totally unclear because the claims are drawn to a method of identifying an agent that inhibits the interaction "between a signal-transducing protein and a cytoplasmic protein, however, part (a) of claims 142 and 143 also recite a compound previously shown to be able to displace the signal-transducing protein bound to the cytoplasmic protein and it is unclear why the method of identifying an agent having a particular activity also includes a compound that has the same activity (i.e., inhibiting the interaction between a signal-transducing protein and a cytoplasmic protein). The examiner acknowledges applicant's intent in part (a) of the claims to define the conditions under which the "contacting" occurs. Consider revising the claims to define the conditions for "contacting" without the inclusion of the "compound previously shown to displace...", since this phrase contradicts the preamble of the claims, i.e., "A method of identifying an agent that inhibits...", making the metes and bounds of the claimed method ambiguous. For example, consider revising base claims 142 and 143 with "under conditions permitting binding between the signal-transducing protein and the cytoplasmic protein or displacement of the signal-transducing protein bound to the cytoplasmic protein, wherein the agent forms a complex with the cytoplasmic protein to which the signal-

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transducing protein is no longer bound;”, or similar language, provided that no new matter is introduced.

10. The rejection of claims 122-132, 140 and applied to newly added claims 142-154 under 35 U.S.C. 103(a) as being unpatentable over Reed et al as evidenced by Niethammer et al in view of Kornau et al is maintained.

The response filed 12/27/2004 has been carefully considered, but is deemed not to be persuasive. The response states that claim 121 has been cancelled and that corresponding new claims 142 and 143 do not encompass the Fas receptor as one of the signal-transducing proteins. Further, the response argues that none of the cited references teach methods using a signal-transducing protein consisting of an amino acid sequence as set forth in SEQ ID Nos:9, 11, 12, 13, 14, 15 and 16 and thus, the cited references do not teach each and every element of the claimed methods. In view of the fact that the peptide sequences set forth in SEQ ID Nos:9, 11, 12, 13, 14, 15 and 16 were isolated from a random peptide library using the Fas-FAP-1 interaction in a yeast two-hybrid assay (see Figure 2 of the specification) and are not sequences of any signal-transducing protein, the claims are being interpreted as being drawn to a method of identifying an agent that inhibits the interaction between a signal-transducing protein and a cytoplasmic protein comprising the amino acid sequence of SEQ ID NO:1. Thus, the claims encompass any signal-transducing protein and any cytoplasmic protein having SEQ ID NO:1 (i.e., GLGF or PDZ domain), which claim language includes the Fas receptor and FAP-1.

The response also argues that the combination of references must teach or suggest each and every element of the claims, must provide some motivation to combine the references and must provide a reasonable expectation of success. In response and in view of the interpretation of the claims as discussed above, Reed et al teach a method of identifying an agent that inhibits the interaction between a FAP protein and Fas, and this method meets each and every element of the claims (see pages 14-15 of the previous Office Action). It is further noted that Reed teaches that FAP contains the amino acid sequence SLGI in one of the GLGF domains (see Figure 14) and thus, FAP is a cytoplasmic protein containing the amino acid sequence of SEQ ID NO:3 (SLGI). Reed does not teach the full scope of signal-transducing proteins or cytoplasmic proteins as encompassed by the claims, however, Kornau et al teach that Fas (also taught by Reed) as well as other signal-transducing receptors have a carboxyl-terminal tSXV motif that interfaces with PDZ domains and it would have been obvious to one of ordinary skill in the art to use the signal-transducing proteins of Kornau in the method of Reed for identifying an agent that interferes with its ability to interact with its respective cytoplasmic protein, since the tSXV-PDZ domain interactions are known to play a general role in connecting receptors and channels to signal-transduction machineries, which carry out essential biological functions (e.g., synaptic plasticity and memory formation) as taught by Kornau and Reed. Further, one of ordinary skill in the art would have had a reasonable expectation of success in doing so because Reed teaches that C-terminal peptides of Fas can associate with a FAP and

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thus, are useful for decreasing the association of a FAP and Fas in a cell by competing for binding to the FAP (see Example II, Figure 8 and column 15, lines 1-13).

Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made and the rejection is maintained.

New Grounds of Rejections

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

11. Claims 122-132, 140 and 142-154 rejected under 35 U.S.C. 101 because the disclosed invention is inoperative and therefore lacks utility.

The claims are drawn to a method of identifying an agent that inhibits the interaction between (i) a signal-transducing protein comprising a peptide selected from the group consisting of amino acid sequences set forth in SEQ ID NOS:9, 11, 12, 13, 14, 15 and 16 and (ii) a cytoplasmic protein comprising the amino acid sequence of SEQ ID NO:1.

The claims encompass using a signal-transducing protein that has a peptide sequence selected from SEQ ID NOS:9, 11, 12, 13, 14, 15 and 16, however, there are no known signal-transducing proteins that have one of these peptides. There is no evidence in applicant's disclosure of a signal-transducing protein comprising one of

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these peptide sequences. Thus, there is no evidence in applicant's disclosure or in the prior art for a signal-transducing protein having a peptide sequence selected from SEQ ID NOS:9, 11, 12, 13, 14, 15 and 16 and therefore, the invention is inoperative. The invention could not and does not work as claimed because the claimed signal-transducing proteins do not exist.

12. Claims 122-132, 140 and 142-154 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the disclosed invention is inoperative and therefore lacks utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

13. Claims 122-132, 140 and 142-154 are rejected under 35 U.S.C. 112, first paragraph, NEW MATTER, as containing subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

The amendments to the claims filed 12/27/2004 have introduced NEW MATTER into the claims. The claims as currently amended are drawn to a signal-transducing protein comprising a peptide selected from the group consisting of amino acid sequences as set forth in SEQ ID NO:9, 11, 12, 13, 14, 15 and 16. The specification discloses signal-transducing proteins comprising the amino acid sequence (S/T)-X-(V/I/L) at the C-terminus (e.g., see page 4, lines 25-32 and Table 1 at page 3). The

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specification does not provide adequate written support for the narrower limitation of a signal-transducing protein comprising an amino acid sequence selected from SEQ ID NOS:9, 11, 12, 13, 14, 15 and 16. Figure 2 shows that the peptides of SEQ ID Nos:9 and 11-16 are peptides selected from a random peptide library using the Fas-FAP-1 interaction in the yeast two-hybrid system. These peptides are not the C-terminal peptide sequence of any signal-transducing protein and applicant has not pointed to anything in the disclosure as-filed providing adequate written support for the instantly claimed signal-transducing proteins comprising a peptide selected from SEQ ID NO:9, 11, 12, 13, 14, 15 and 16. Thus, the instant claims now recite limitations, which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the claims, which did not appear in the specification, as-filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicant is required to provide sufficient written support for the limitations recited in present claims in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

14. Claims 122-132, 140 and 142-154 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of identifying an agent that inhibits the interaction between (i) a signal-transducing protein comprising a peptide selected from the group consisting of amino acid sequences set forth in SEQ ID NOS:9, 11, 12, 13, 14, 15 and 16 and (ii) a cytoplasmic protein comprising the amino acid sequence of SEQ ID NO:1.

The claims encompass signal-transducing proteins comprising the peptide sequence of SEQ ID NO:9, 11, 12, 13, 14, 15 or 16. The specification provides insufficient written description to support the genus of signal-transducing proteins encompassed by the claims because the specification does not disclose a single signal-transducing protein comprising a peptide sequence selected from SEQ ID NOS:9, 11, 12, 13, 14, 15 or 16. Further, a sequence search of SEQ ID NOS:9 and 11-16 in all relevant databases (i.e., non-patent and patent literature) did not produce a sequence match or identify any known signal-transducing protein having these peptide sequences.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of signal-transducing proteins, and therefore conception is not

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achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only signal-transducing proteins comprising the sequence set forth in SEQ ID NO:4 ((S/T)-X-(V/I/L)), of the claimed methods meet the written description provision of 35 U.S.C. §112, first paragraph

Conclusions

15. No claim is allowed.

16. Applicant's amendment necessitated the new grounds of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within


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TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,
David J. Blanchard
571-272-0827


LARRY R. HELMS, PH.D
PRIMARY EXAMINER